
Methyl Salicylate

CAS #119-36-8

Swiss CD-1 mice, at 0.0, 25, 50, and 100 mg/kg by gavage

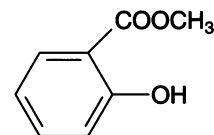
James Lamb IV, NTP/NIEHS Project Officer,

Jerry R. Reel, Rochelle Tyl, and A. Davis Lawton,

Research Triangle Institute

Started 3/17/82; Completed 7/30/84

NTIS #PB84241140



Methyl salicylate (MS) is used as a fragrance and flavoring agent but is lethal at sufficient doses and is teratogenic in rodents. MS was tested to update and expand the reproductive toxicity database, and used, in part, as a known positive: this is the second of two simultaneous studies conducted at different laboratories, using the RACB protocol and Swiss CD-1 mice (Morrissey et al., *Fundam Appl Toxicol* 13:747-777 [1989]). Food and water consumptions, clinical signs, and body weights were used in the Task 1 dose-range-finding study to set doses for the continuous cohabitation phase (Task 2) at 25, 50, and 100 mg/kg/day by gavage in corn oil.

Deaths occurred at a rate of two, one, five, and three mice in the control to high dose groups, respectively. Some of these

deaths were apparently due to gavage trauma; the cause of death was not determined in the remaining cases.

MS exposure had no effect on parental body weights or clinical signs.

There was no adverse effect of MS exposure on the reproductive end points measured in Task 2. Since there were no treatment-related changes, no Task 3 was conducted.

The last litter in Task 2 from the control and high dose groups was reared by the dams until weaning (postnatal day 21), and then dosed with MS until the Task 4 mating at approximately postnatal day 74. There were no reductions in pup viability or weight during nursing and no differences between treated and control mice before and during the week of mating in Task 4.

In the single mating that comprises Task 4, there were no MS-related changes in the number of pups per litter, their viability or sex ratio, or their body weight adjusted for litter size.

After the F₂ litters were evaluated, all animals were killed and the F₁ adults necropsied. For males and females, there were no effects on body weights or organ weights. The percent motile, density, and percent morphologically abnormal end points were all unchanged for epididymal sperm. No estrous cyclicity evaluation was performed.

At the doses used for this study (which were 20% the dose used in the previous positive study), methyl salicylate caused no adverse effects on body weight or reproductive indices in either the first or second generation.

METHYL SALICYLATE

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB84241140

Chemical: Methyl Salicylate

CAS#: 119-36-8

Mode of exposure: Gavage

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	25 mg/kg	50 mg/kg	100 mg/kg
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, —
Kidney weight ^a		•	•	•
Liver weight ^a		•	•	•
Mortality		—	—	—
Feed consumption		•	•	•
Water consumption		•	•	•
Clinical signs		—	—	—

Reproductive toxicity			
̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight ^a	•	•	•
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F ₁ generation	Dose concentration →	•	•	100 mg/kg
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		•	•	—, —
Mortality		•	•	—, —
Adult body weight		•	•	—, —
Kidney weight ^a		•	•	•
Liver weight ^a		•	•	—, —
Feed consumption		•	•	•
Water consumption		•	•	•
Clinical signs		•	•	—, —

Reproductive toxicity			
Fertility index	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Absolute testis, epididymis weight ^a	•	•	—, —
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	•

Summary information	
Affected sex?	Unclear
Study confounders:	None
F ₁ more sensitive than F ₀ ?	No
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.